

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
23 June 2005 (23.06.2005)

PCT

(10) International Publication Number  
**WO 2005/055980 A2**

- (51) International Patent Classification<sup>7</sup>: **A61K 9/00**
- (21) International Application Number:  
PCT/US2004/040660
- (22) International Filing Date: 3 December 2004 (03.12.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/527,330 5 December 2003 (05.12.2003) US
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- (81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.
- (84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,  
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— without international search report and to be republished  
upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: POLYMALIC ACID-BASED MULTIFUNCTIONAL DRUG DELIVERY SYSTEM

(57) Abstract: A structured drug system that is useful for delivering a drug payload to a specific tissue or cell type is disclosed. The system is based on purified polymalic acid. This polymer isolated from natural sources is biocompatible, biodegradable and of very low toxicity. The polymer is extremely water soluble and contains a large number of free carboxyl groups which can be used to attach a number of different active molecules. In the examples disclosed N-hydroxysuccinimide esters of the carboxyl groups are used to attach such molecules. The active molecules include monoclonal antibodies to promote specific cellular uptake and specific pro-drugs such as antisense nucleic acids designed to modify the cellular metabolism of a target cell. The pro-drugs are advantageously linked by a somewhat labile bond so that they will be released under specific conditions. In addition, the system contains amide-linked valine to encourage membrane disruption under lysosomal conditions. Polyethylene glycol groups are attached to extend the drug system's circulation half-life. In addition, fluorescent reported groups can be readily included to aid in visualizing and confirming drug system targeting. The drug system can deliver treatments for a wide range of diseases and is specially advantageous for treatment of neoplasms.

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